UNITED STATES DISTRICT COURT
EASTERN DISTRICT OF VIRGINIA
ALEXANDRIA DIVISION

GILDA HAGAN-BROWN Plaintiff, v. ELI LILLY AND COMPANY, an Indiana corporation, Defendant.	CASE NO.: 1:14-CV-01614
JANINE ALI Plaintiff, v. ELI LILLY AND COMPANY, an Indiana corporation, Defendant.	CASE NO.: 1:14-CV-01615

MOTION FOR JUDGMENT ON THE PLEADINGS
AND
MEMORANDUM OF LAW IN SUPPORT

PRELIMINARY STATEMENT

In their lawsuits against Eli Lilly and Company ("Lilly"), Plaintiffs Janine Ali and Gilda Hagan-Brown have asserted identical claims that, among other theories, Lilly's Cymbalta medicine was defectively designed. Specifically, Plaintiffs claim that Cymbalta's distribution in its only approved form — 20-, 30-, and 60-milligram capsules — is defective because it does not allow for doses below 20 milligrams, which Plaintiffs claim increases the likelihood of discontinuation symptoms. These claims, which Lilly denies, are necessarily preempted by federal law. Pursuant to the United States Supreme Court's decisions in *PLIVA, Inc. v. Mensing* and *Mutual Pharmaceutical Co. v. Bartlett*, a state-law design defect claim is preempted — and thus fails as a matter of law — if it would require the defendant to take action it could not unilaterally take without the approval of a federal agency. Here, federal law prohibits pharmaceutical manufacturers from altering the dosage form or composition of any medication without first seeking the approval of the federal Food and Drug Administration through a complex regulatory process. This regulatory framework therefore extinguishes Plaintiffs' efforts to require changes to Cymbalta's dosing or composition through state-law product liability claims.

Thus, even if all of Plaintiffs' allegations were accepted as true, their design defect claims would fail as a matter of law under binding preemption principles. Lilly therefore moves for judgment on the pleadings, seeking dismissal of Plaintiffs' design defect claims with prejudice.

FACTUAL ALLEGATIONS

In 2004, the federal Food and Drug Administration ("FDA" or "Agency") approved Cymbalta (duloxetine) for treatment of major depressive disorder. *See Ali* Complaint, Dkt. No. 1, ¶ 12; *Hagan-Brown* Complaint, Dkt. No. 1, ¶ 12. The Agency subsequently approved new indications for generalized anxiety disorder (in 2007) and fibromyalgia (in 2008). *See Ali*

Complaint, Dkt. No. 1, ¶ 12; *Hagan-Brown* Complaint, Dkt. No. 1, ¶ 12. Since the medicine's launch in 2004, the FDA has approved Cymbalta only for manufacture and distribution in 20-, 30- or 60-milligram capsules containing enteric-coated pellets of duloxetine hydrochloride. *See Ali* Complaint, Dkt. No. 1, ¶¶ 1, 19, 24, 48; *Hagan-Brown* Complaint, Dkt. No. 1, ¶¶ 1, 19, 24, 48.[1] Plaintiffs do not allege that the FDA has ever approved Cymbalta for manufacture or distribution in any form other than 20-, 30-, or 60-milligram capsules containing enteric-coated pellets of the medicine.

In support of their design defect claims (labeled "Second Cause of Action — Design Defect" in each Complaint), Plaintiffs allege that the capsules for Cymbalta are defective because: (1) the company does not produce them in doses smaller than 20 milligrams; and (2) the capsules cannot be split or opened to permit a patient to fashion a smaller dose from a single capsule. *See Ali* Complaint, Dkt. No. 1, ¶¶ 19, 24, 48-49; *Hagan-Brown* Complaint, Dkt. No. 1, ¶¶ 19, 24, 48-49. According to Plaintiffs, these alleged design problems hinder a patient's ability to taper off of the medicine because a patient cannot take a dose smaller than 20 milligrams. *See Ali* Complaint, Dkt. No. 1, ¶¶ 19, 24, 48-49; *Hagan-Brown* Complaint, Dkt. No. 1, ¶¶ 19, 24, 48-

[1] Cymbalta's FDA-approved dosage form is also readily apparent in the medicine's FDA-approved labeling, which is a matter of public record and available online via the FDA's web site. *See* Cymbalta Package Insert (Sept. 2011 version), Ex. 1 to the Declaration of Jeffrey T. Bozman ("Bozman Decl."), *available at* http://www.accessdata.fda.gov/drugsatfda_docs/label/2011/021427s039lbl.pdf. Although it is not necessary for the Court to review the labeling to resolve Lilly's motion (since the relevant facts are alleged in Plaintiffs' Complaints), the Court may take judicial notice of the labeling when ruling on Lilly's motion for judgment on the pleadings. *See, e.g., Sec'y of State for Defence v. Trimble Navigation Ltd.*, 484 F.3d 700, 705 (4th Cir. 2007) (when ruling on dismissal motion, court may take judicial notice of matters of public record and documents that are integral to complaint and authentic). That the labeling is integral to Plaintiffs' Complaints is beyond question, since Plaintiffs cite and quote the labeling repeatedly in their pleadings. *See Ali* Complaint, Dkt. No. 1, ¶¶ 1, 15, 16, 18, 20, 21, 22, 25, 26; *Hagan-Brown* Complaint, Dkt. No. 1, ¶¶ 1, 15, 16, 18, 20, 21, 22, 25, 26.

49. In turn, Plaintiffs allege, patients cannot discontinue the medicine gradually and therefore are more likely to suffer alleged discontinuation side effects. *See Ali* Complaint, Dkt. No. 1, ¶¶ 19, 24, 48-49; *Hagan-Brown* Complaint, Dkt. No. 1, ¶¶ 19, 24, 48-49. Ultimately, the essence of Plaintiffs' design defect claims is that, instead of designing, manufacturing, and distributing Cymbalta in its only FDA-approved form (20-, 30-, or 60-milligram capsules), Lilly should have designed and produced the medicine in capsules containing smaller doses, or in "scored tablets that can be halved and quartered with relative ease," or in "liquid form which can be measured and dispensed in small increments." *See Ali* Complaint, Dkt. No. 1, ¶ 19; *Hagan-Brown* Complaint, Dkt. No. 1, ¶ 19.

Because federal law preempts Plaintiffs' design defect claims even if all of Plaintiffs' allegations are taken as true, those claims are ripe for resolution at this stage. Indeed, prior decisions in this litigation have resolved Cymbalta issues as a matter of law. *See McDowell v. Eli Lilly & Co.*, — F. Supp. 3d —, 2014 WL 5801604, at *15 (S.D.N.Y. 2014) ("Taken together, the Cymbalta warning is adequate as a matter of law because it is accurate, clear, consistent on its face and portrays with sufficient intensity the risk involved in taking the drug.") (citation and quotation marks omitted), *reconsideration denied*, 2015 WL 845720, at *7 (S.D.N.Y. Feb. 25, 2015); *Carnes v. Eli Lilly & Co.*, 2013 WL 6622915, at *7 (D.S.C. Dec. 16, 2013) (granting judgment as a matter of law because plaintiff could not establish that any alleged defect in Cymbalta's warnings proximately caused plaintiff's injuries).

LEGAL STANDARD

Pursuant to Federal Rule of Civil Procedure 12(c), a motion for judgment on the pleadings may be brought at any time after the pleadings are closed, so long as the motion is filed early enough not to delay trial. *See* Fed. R. Civ. P. 12(c). When ruling on a motion for judgment on the pleadings, the Court applies the same standard it applies when ruling on a

motion to dismiss under Rule 12(b)(6). *See Drager v. PLIVA USA, Inc.*, 741 F.3d 470, 474 (4th Cir. 2014). Accordingly, judgment on the pleadings shall be granted if, after accepting all well-pleaded allegations as true, the Court concludes that "the plaintiff cannot prove any set of facts in support of his claim entitling him to relief." *Id.* (quoting *Edwards v. City of Goldsboro*, 178 F.3d 231, 244 (4th Cir. 1999)); *see also Sherman v. Litton Loan Servicing, L.P.*, 796 F. Supp. 2d 753, 757-58 (E.D. Va. 2011).

The question of whether a pharmaceutical plaintiff's claims are preempted by federal law may be resolved on a motion for judgment on the pleadings. *See Drager*, 741 F.3d at 474, 477-79 (affirming district court's Rule 12(c) dismissal of pharmaceutical plaintiff's design defect and other tort claims on preemption grounds). Under the United States Constitution's Supremacy Clause, the laws and treaties of the United States "shall be the supreme Law of the Land . . . , any Thing in the Constitution or Laws of any State to the Contrary notwithstanding." U.S. Const. art. VI, cl. 2. Therefore, state laws that conflict with federal law are "without effect." *Mut. Pharm. Co. v. Bartlett*, 133 S. Ct. 2466, 2473 (2013) (quoting *Maryland v. Louisiana*, 451 U.S. 725, 746 (1981)). Even in the absence of an express preemption provision, a state law is impliedly preempted where it is "impossible for a private party to comply with both state and federal requirements." *Bartlett*, 133 S. Ct. at 2473 (quoting *English v. Gen. Elec. Co.*, 496 U.S. 72, 79 (1990)).

LEGAL ARGUMENT

Even if the Court accepts all of Plaintiffs' allegations as true, their design defect claims necessarily fail as a matter of law under well-established principles of preemption. As an initial matter, federal law prohibits Lilly from unilaterally implementing the alternative design that Plaintiffs propose. This in turn requires dismissal because, pursuant to Supreme Court

precedent, a state-law design defect claim is preempted if it would impose a requirement that the defendant could not meet without first seeking federal agency approval.

I. Lilly Could Not Unilaterally Alter Cymbalta's Dosing or Composition Without Violating Federal Law.

In support of their state-law design defect claims, Plaintiffs allege that, instead of designing, manufacturing, and distributing Cymbalta in its only FDA-approved forms (20-, 30-, or 60-milligram capsules), Lilly should have designed and produced the medicine in capsules containing smaller doses or in a different dosage form entirely, such as a tablet or a liquid. *See Ali* Complaint, Dkt. No. 1, ¶¶ 19, 24, 48-49; *Hagan-Brown* Complaint, Dkt. No. 1, ¶¶ 19, 24, 48-49. Importantly, however, Lilly could not unilaterally implement Plaintiffs' proposed alternative design without violating federal law.

Under federal law, a pharmaceutical manufacturer must obtain approval from the FDA before marketing a new medicine in interstate commerce. 21 U.S.C. § 355(a). In the case of a brand-name medicine like Cymbalta, a manufacturer can secure such FDA approval only by submitting a new drug application ("NDA"). An NDA is a voluminous compilation of materials that must include, among other things, results of clinical trials, the proposed labeling for the medicine, a discussion of why the medicine's benefits exceed its risks for the proposed indications, and a full description of the medicine's "composition, manufacture, and specification[s]," including its dosage form and strength. *See* 21 U.S.C. § 355(b)(1); 21 C.F.R. § 314.50(a)&(d); *see also Mut. Pharm. Co. v. Bartlett*, 133 S. Ct. 2466, 2470-71 (2013) (describing NDA process as "onerous and lengthy").

Once a medicine is approved, the manufacturer is prohibited from unilaterally making any "changes in the qualitative or quantitative formulation of the drug product, including active ingredients, or in the specifications provided in the approved application." 21 C.F.R. §

314.70(b)(2)(i); *Bartlett*, 133 S. Ct. at 2471. Rather, the manufacturer may make any such changes only by submitting a supplemental new drug application ("sNDA") and again securing FDA approval through an onerous review process. *See* 21 C.F.R. § 314.70(b)(3). Changes that require such pre-approval include qualitative or quantitative changes to a medicine's dosage form, such as a change in dose strength or a conversion from a capsule to a tablet or a liquid. *See* 21 C.F.R. § 314.70(b)(2)(i) (stating that changes in "qualitative or quantitative formulation" of "drug product" require pre-approval); 21 C.F.R. § 314.3 (defining "drug product" as "a finished dosage form, for example, tablet, capsule, or solution, that contains a drug substance"); *see also* 21 U.S.C. § 356a(c)(2)(A) (change in "qualitative or quantitative formulation of the drug" is "major change" requiring pre-approval). In fact, regulatory guidance materials from the FDA suggest that changes such as those Plaintiffs have proposed might even require the submission and approval of an entirely new NDA — as opposed to an sNDA. *See* FDA, Guidance for Industry: Submitting Separate Marketing Applications and Clinical Data for Purposes of Assessing User Fees (Dec. 2004), Bozman Decl. Ex. 2, at 5, *available at* http://www.fda.gov/downloads/Drugs/GuidanceComplianceRegulatoryInformation/Guidances/UCM079320.pdf (recommending that change in dosage form "be submitted as a separate original application").[2]

If a manufacturer circumvents these legally mandated processes by unilaterally altering the composition of its medicine, it becomes subject to federal enforcement action. Indeed, a manufacturer that flouts these processes may be subject to criminal prosecution. *See* 21 U.S.C.

[2] Like Cymbalta's labeling, FDA guidance documents are matters of public record that the Court may consider when ruling on a motion for judgment on the pleadings. *See, e.g., Sec'y of State for Defence*, 484 F.3d at 705.

§§ 331(d) & 333(a) (imposing criminal sanctions for introducing unapproved drugs into interstate commerce).

In light of these legal requirements, there can be no question that Lilly could not unilaterally manufacture and distribute Cymbalta in a new dosage form or strength. Even if it were technically feasible, the alternative design that Plaintiffs claim is required under state law — that is, distribution in capsules containing smaller doses or in a tablet or liquid form — would require, among other things, review and pre-approval by the FDA.

II. Because Plaintiffs' Proposed Design Changes Would Require FDA Review and Approval, Their Design Defect Claims Are Preempted.

Because Lilly could not unilaterally implement the alternative design that Plaintiffs claim is required under state law,[3] Plaintiffs' design defect claims are preempted by federal law and must therefore fail even if all of Plaintiffs' allegations are true. Decisions of the United States Supreme Court make clear that, where state law would require action that a pharmaceutical manufacturer could not take without the FDA's prior approval, the state requirement must yield under principles of "impossibility preemption." *See PLIVA, Inc. v. Mensing*, 131 S. Ct. 2567, 2580-81 (2011); *Mut. Pharm. Co. v. Bartlett*, 133 S. Ct. 2466, 2476-77 (2013).[4]

[3] As noted in its Answers to Plaintiffs' Complaints, Lilly denies that Plaintiffs can prove a claim of design defect under the substantive law of Virginia or any other state. *See* Answer to *Ali* Complaint, Dkt. No. 5, ¶¶ 1, 19, 24, 44-52 (denying design defect allegations); Answer to *Hagan-Brown* Complaint, Dkt. No. 5, ¶¶ 1, 19, 24, 44-52 (same). However, solely for purposes of resolving the preemption issue on the pleadings, and without waiving its right to later challenge the viability of Plaintiffs' claims under state law, Lilly assumes for this motion only that Plaintiffs' design defect claims could proceed under state law.

[4] The preemption issue is particularly ripe for resolution now, as Plaintiffs recently noticed a 30(b)(6) deposition requesting extensive company testimony on the "design and dosing of the Cymbalta capsule." In light of the non-viability of Plaintiffs' design defect claims, Lilly plans to oppose Plaintiffs' efforts to seek discovery on design-related issues.

In *PLIVA, Inc. v. Mensing*, the Supreme Court considered a failure-to-warn suit in which plaintiffs alleged that a generic manufacturer of metoclopramide failed to provide an adequate warning of the risk of tardive dyskinesia, a neurological disorder. 131 S. Ct. at 2572-73. The defendant argued that the plaintiffs' claims were preempted because, under federal law, generic medicine labels must at all times remain identical to the labels for their brand-name counterparts, meaning that the manufacturer could not unilaterally make the labeling changes the plaintiffs claimed were required under state law. *Id.* at 2573. The Supreme Court agreed, and in so doing articulated the impossibility preemption principle that applies with equal force here:

> Before the Manufacturers could satisfy state law, the FDA — a federal agency — had to undertake special effort permitting them to do so. *To decide these cases, it is enough to hold that when a party cannot satisfy its state duties without the Federal Government's special permission and assistance, which is dependent on the exercise of judgment by a federal agency, that party cannot independently satisfy those state duties for preemption purposes.*
>
> Here, state law imposed a duty on the Manufacturers to take a certain action, and federal law barred them from taking that action. The only action the Manufacturers could independently take — asking for the FDA's help — is not a matter of state-law concern. [The plaintiffs'] tort claims are pre-empted.

Id. at 2580-81 (emphasis added).

In 2013, two years after *Mensing* was decided, the Supreme Court held in the *Bartlett* case that the rule of *Mensing* also preempts design defect claims. *See Bartlett*, 133 S. Ct. at 2470. In reaching this conclusion, the Supreme Court reasoned that any state law that requires alteration of a medicine's composition necessarily conflicts with federal law that prohibits a manufacturer from unilaterally altering the composition of its product. *See id.* at 2478-79 ("[W]e hold that state-law design defect claims like New Hampshire's that place a duty on manufacturers to render a drug safer by either altering its composition or altering its labeling are

in conflict with federal laws that prohibit manufacturers from unilaterally altering drug composition or labeling.").

In the wake of *Mensing* and *Bartlett*, plaintiffs bringing design defect claims against brand-name manufacturers have attempted to circumvent the Supreme Court's holdings by arguing that they apply only in cases involving generic manufacturers. This argument is easily rejected for two reasons. ***First***, *Mensing* and *Bartlett* were decided on the basis of a clear preemption rule that, on its face, is not in any way limited to the generics context. *See Mensing*, 131 S. Ct. at 2580-81 ("To decide these cases, it is enough to hold that when a party cannot satisfy its state duties without the Federal Government's special permission and assistance, which is dependent on the exercise of judgment by a federal agency, that party cannot independently satisfy those state duties for preemption purposes."); *see also Bartlett*, 133 S. Ct. at 2471, 2479 ("Once a drug — *whether generic or brand-name* — is approved, the manufacturer is prohibited from making any major changes to the qualitative or quantitative formulation of the drug product, including active ingredients, or in the specifications provided in the approved application.") (emphasis added) (quotation marks omitted).

Second, since the *Mensing* and *Bartlett* decisions came down, other courts have applied those decisions to conclude that claims against brand-name manufacturers are preempted for the same reason that such claims against generic manufacturers are preempted: under the applicable federal regulatory framework, it is impossible for *any* pharmaceutical manufacturer — generic or brand-name — to take certain actions (including alteration of the design of its product) without first seeking FDA approval. *See Yates v. Ortho-McNeil Pharm., Inc.*, — F. Supp. 3d —, 2015 WL 66423, at *5-7 (N.D. Ohio 2015) (relying on *Bartlett* to conclude that design defect claim against manufacturer of brand-name birth control patch was preempted: "Although Ms. Yates'

attorneys assert that the preemption is applicable to only generic drugs, the language in *Bartlett* and *Amos* is not so restrictive."); *Booker v. Johnson & Johnson*, — F. Supp. 3d —, 2014 WL 5113305, at *2, *4-5 (N.D. Ohio 2014) (relying on *Bartlett* to conclude that design defect claim against manufacturer of brand-name birth control patch was preempted: "[I]t was impossible for the Defendants to comply with both its state-law duty to alter the composition of the drug, and its federal-law duty not to alter an FDA-approved design. Accordingly, Plaintiff's design defect claim fails as a matter of law."); *Amos v. Biogen Idec Inc.*, 28 F. Supp. 3d 164, 169 (W.D.N.Y. 2014) (relying on *Bartlett* to conclude that design defect claims against manufacturer of brand-name multiple sclerosis medicine were preempted: "[T]he [Supreme] Court held that because a drug manufacturer could not simultaneously comply with FDA requirements mandating the specific design of an approved drug and state-law requirements mandating that the design be altered, the state-law requirements were preempted by federal law."); *Thompson v. Allergan USA, Inc.*, 993 F. Supp. 2d 1007, 1013-14 (E.D. Mo. 2014) (relying on *Mensing* and *Bartlett* to find state-law claims preempted where plaintiffs alleged that manufacturer of brand-name prescription eye medication should have distributed medicine in vials containing smaller quantities: "*Bartlett* extended the holding of [*Mensing*] to cover not just failure-to-warn claims, but also those claims that would require a redesign of a drug."); *see also In re Celexa & Lexapro Mktg. & Sales Practices Litig.*, 779 F.3d 34, 35, 40-43 (1st Cir. 2015) (relying on *Mensing* and *Bartlett* to hold that consumer fraud claims against brand-name manufacturer failed under principles of impossibility preemption).

As support for their anticipated generics-only argument, Plaintiffs will likely point to the Supreme Court's earlier decision in *Wyeth v. Levine*, in which the Court allowed a labeling-based failure-to-warn claim to proceed against a brand-name manufacturer. 555 U.S. 555, 581 (2009).

In that case, however, the Supreme Court explicitly concluded that compliance with state law was not impossible because of a federal regulation — the "changes being effected" ("CBE") regulation — that permits brand-name manufacturers to make safety-based labeling changes (without prior approval) under narrow circumstances. *See id.* at 568-73. *Levine* does nothing to alter the outcome here, since neither the CBE regulation nor any other regulation would permit Lilly to implement Plaintiffs' proposed dosage form changes without the FDA's prior approval. Indeed, the case law makes clear that *Levine* controls only where the manufacturer could implement the proposed changes unilaterally — without the FDA's prior approval or assistance. *See In re Celexa & Lexapro*, 779 F.3d at 41 (finding claims preempted in brand-name case: "The [Supreme] Court thus limited *Wyeth* to situations in which the drug manufacturer can, of its own volition, strengthen its label in compliance with its state tort duty.") (quotation marks omitted).

Applying these preemption rules here compels the conclusion that Plaintiffs' design defect claims against Lilly are preempted by federal law — even if all of the allegations in their Complaints are assumed to be true. As explained above, it is beyond dispute that Lilly could not implement the alternative designs Plaintiffs claim are required by state law — that is, distribution of Cymbalta in capsules containing smaller doses or in a tablet or liquid form — without first following the "onerous and lengthy" regulatory process, filing a new application, and seeking the approval of the FDA. *See Bartlett*, 133 S. Ct. at 2470-71 (citing statutes and regulations). In other words, Lilly could not "satisfy its state duties without the Federal Government's special permission and assistance, which is dependent on the exercise of judgment by a federal agency." *Mensing*, 131 S. Ct. at 2580-81. Because it would have been impossible for Lilly to

simultaneously comply with its supposed state-law duties and its duties under federal law, Plaintiffs' design defect claims must fail under principles of preemption.

CONCLUSION

For the foregoing reasons, Plaintiffs' design defect claims are preempted by federal law. The Court should therefore grant Lilly's motion for judgment on the pleadings and dismiss Plaintiffs' design defect claims with prejudice.

Dated April 10, 2015

Respectfully submitted,

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CERTIFICATE OF SERVICE

I hereby certify that on the 10th day of April, 2015, I will electronically file the foregoing with the Clerk of the Court using the CM/ECF system, which will then send a notification of such filing (NEF) to the following:

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